A Combined Prediction Model for Biliary Tract Cancer using the Prognostic Nutritional Index and Pathological Findings: A Single-center Retrospective Study

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Abstract

Background: The prognostic nutritional index, a marker of nutritional status and systemic inflammation, is a known biomarker for various cancers. However, few studies have evaluated the predictive value of the prognostic nutritional index in patients with biliary tract cancer. Therefore, we investigated the prognostic significance of the prognostic nutritional index and developed a risk-stratification system to identify prognostic factors in patients with biliary tract cancer.

Methods: Between July 2010 and March 2021, 117 patients with biliary tract cancer were recruited to this single-center retrospective study. The relationship between clinicopathological variables, including the prognostic nutritional index and overall survival, was analyzed using univariate and multivariate analyses. $P < 0.05$ was considered statistically significant.

Results: The median age was 75 (range, 38–92) years. Thirty patients had intrahepatic cholangiocarcinoma; 29, gallbladder carcinoma; 28, distal cholangiocarcinoma; 16, ampullary carcinoma; and 13, perihilar cholangiocarcinoma. R0 resection was achieved in 99 patients. In univariate analysis, the prognostic nutritional index (< 42), lymph node metastasis, carbohydrate antigen 19-9 level (> 20 U/mL), preoperative cholangitis, tumor differentiation, operation time (≧ 360 minutes), and R1–2 resection were significant risk factors for overall survival. The prognostic nutritional index ($P = 0.007$), lymph node metastasis ($P = 0.024$), and tumor differentiation ($P = 0.008$) were independent prognostic factors in the multivariate analysis. A combined score of the prognostic nutritional index and pathological findings outperformed each marker alone, in terms of discriminatory power.

Conclusions: The prognostic nutritional index, lymph node metastasis, and tumor differentiation were independent prognostic predictors after surgical resection in patients with biliary tract cancer. A combined prediction model using the prognostic nutritional index and pathological findings accurately predicted prognosis and can be applied as a novel prognostic indicator for patients with biliary tract cancer.

Background

Biliary tract cancer (BTC), including gallbladder carcinoma (GBC), cholangiocarcinoma, and ampullary carcinoma, is a relatively rare, but aggressive malignancy [1]. Despite its rarity, the incidence of BTC has steadily increased in recent decades [1]. Radical resection is the only curative treatment option for BTC. However, the high recurrence rate is a major concern [2]. Moreover, BTC is usually diagnosed at an advanced stage, at which point most patients cannot be considered as candidates for radical resection. Despite recent developments in surgical techniques and adjuvant chemotherapy, the prognosis remains poor [3, 4]. Preoperative prognostic markers for BTC may allow better risk-benefit assessment before surgery and permit patient stratification for more individualized treatment [5]. Therefore, it is essential to identify new predictive biomarkers.

The prognostic nutritional index (PNI) is a marker of nutritional status and systemic inflammation based on serum albumin concentration and total lymphocyte count, both of which can be easily obtained from

routine preoperative blood tests [6]. Several studies [7–11] have shown that the PNI can be used as a prognostic indicator in patients with various cancers. However, few studies have evaluated the prognostic value of the PNI in patients with BTC. Therefore, in this single-center retrospective study, we investigated the prognostic significance of the PNI in patients with BTC and explored its potential clinical application. Additionally, we developed a risk-stratification system combining clinicopathological predictors to identify prognostic factors in patients with BTC.

Methods

Patients

A total of 117 consecutive patients who underwent surgical resection for BTC in the Department of Surgery, National Hospital Organization Fukuyama Medical Center (Hiroshima, Japan) between July 2010 and March 2021 were retrospectively reviewed. BTC included GBC, intrahepatic cholangiocarcinoma (ICC), distal cholangiocarcinoma, ampullary carcinoma, and perihilar cholangiocarcinoma, as confirmed by imaging and pathological findings.

Data collection

Clinicopathological data were obtained retrospectively from patients' medical records, including demographic information (age at surgery and sex), laboratory data (serum C-reactive protein level, albumin concentration, platelet count, neutrophil count, lymphocyte count, and tumor markers), comorbidities (hypertension, diabetes mellitus, cardiac disease, and stroke), preoperative cholangitis, operative procedure (i.e., type of resection), operative blood loss, operation time, transfusion, tumor stage (Union for International Cancer Control Tumor–Node–Metastasis [TNM] classification [sixth edition]) [12], tumor differentiation, and postoperative adjuvant chemotherapy. Curative (R0) resection was defined as complete removal of all macroscopic nodules with microscopically clear margins. R1 and R2 resections were defined as microscopic or macroscopic disease, respectively, involving ≥ 1 margin. Complications were defined according to the Clavien–Dindo classification [13]. In this study, postoperative complications were defined as complications of Clavien–Dindo grade ≥ 3a. Postoperative mortality was defined as death from any cause within 30 days after surgery.

PNI evaluation

Peripheral venous blood samples were collected within 2 weeks before surgery. The PNI was calculated as follows: 10 × serum albumin concentration (g/dL) + 0.05 × total lymphocyte count (/mm^3) [6, 14].

Follow-up

All patients underwent routine follow-up until March 2021. Postoperative follow-up included medical history (symptoms and physical examination), laboratory tests, and imaging studies performed every 6 months for ≥ 5 years. Patients with lymph node metastasis or who underwent R1–2 resection received

postoperative adjuvant chemotherapy (tegafur/gimeracil/oteracil) for approximately 6 months. None of the patients received neoadjuvant chemotherapy.

Outcomes

Overall survival (OS) was defined as the interval between the date of surgery and the date of death or last follow-up. The relationship between clinicopathological variables, including the PNI and OS, was analyzed using univariate and multivariate analyses. A combined prediction model was developed using independent prognostic factors. The area under the receiver operating characteristic curve (AUC) was calculated to compare the predictive ability of each scoring system.

Statistical analyses

Data are expressed as the mean ± standard deviation. Univariate analysis was performed using the Mann–Whitney *U* test and Chi-square test. Diagnostic accuracy was determined using the AUC method. The optimal cutoff value of the PNI was determined by maximizing the Youden index (sensitivity + specificity − 1) [15]. OS and disease-free survival rates were estimated using the Kaplan–Meier method and compared using the log-rank test. Univariate and multivariate analyses were performed using the Cox proportional hazards model. Prognostic factors that were statistically significant in the univariate analysis were included in the multivariate analysis. All statistical analyses were conducted using JMP (Version 11; SAS Institute, Cary, NC, USA). Statistical significance was defined as $P < 0.05$.

Results

Patient characteristics

Patient characteristics are summarized in Table 1. The median age was 75 (range, 38–92) years. Thirty patients had ICC; 29, GBC; 28, distal cholangiocarcinoma; 17, ampullary carcinoma; and 13, perihilar cholangiocarcinoma. R0 resection was achieved in 99 patients. Operative procedures included cholecystectomy in 11 patients, bile duct resection without hepatectomy in one, liver resection in 59 (liver bed resection [n = 7], partial hepatectomy [n = 1], subsegmentectomy [n = 11], sectionectomy [n = 6], hemihepatectomy [n = 31], and trisectionectomy [n = 3]), pancreaticoduodenectomy in 43, and hepatopancreaticoduodenectomy in two. None of the patients received neoadjuvant chemotherapy or underwent preoperative portal vein embolization. Postoperative complications were observed in 44 of 117 patients: pancreatic fistula in 23 patients, bile leakage in eight, abdominal abscess in eight, pleural effusion in two, abdominal bleeding in one, chylous ascites in one, and heart failure due to arrhythmia in one. One patient died of heart failure due to arrhythmia on postoperative day 18; thus, the mortality rate was 0.9%. The optimal cutoff value of the PNI was 42. Patients were stratified into a high PNI (≥ 42) group (n = 88; 75.2%) and a low PNI (< 42) group (n = 29; 24.8%) according to the cutoff value.

Table 1
Patient characteristics

Characteristic	Patients
Age (years), mean ± SD (range)	74.0 ± 9.51 (39–92)
Sex (male/female)	73/44
BMI (kg/m^2), mean ± SD (range)	22.41 ± 3.68 (14.20–32.46)
Preoperative laboratory data, mean ± SD (range)	
Albumin concentration (g/dL)	3.78 ± 0.53 (1.70–4.80)
Platelet count (×10^4/mm^3)	21.62 ± 66.26 (3.37–46.30)
Neutrophil count (×10^3/mm^3)	3.78 ± 1.91 (1.01–15.39)
Lymphocyte count (×10^3/mm^3)	1.58 ± 0.71 (0.48–5.80)
CRP level (mg/dL)	1.11 ± 2.76 (0.01–24.18)
CEA level (ng/mL)	5.98 ± 13.07 (0.56–113.06)
CA19-9 level (U/mL)	1 013.91 ± 4 139.26 (2.00–39 284.20)
PNI	45.75 ± 6.52 (22.21–62.98)
Type of cancer, n (%)	30 (25.6)
Intrahepatic cholangiocarcinoma	29 (24.8)
Gallbladder carcinoma	28 (23.9)
Distal cholangiocarcinoma	17 (14.5)
Ampullary carcinoma	13 (11.1)
Perihilar cholangiocarcinoma	
Preoperative cholangitis, n (%)	44 (37.6)
Comorbidities (absent/present)	33/84

BMI, body mass index; CA19-9, carbohydrate antigen 19 – 9; CEA, carcinoembryonic antigen; CRP, C-reactive protein; PNI, prognostic nutritional index; SD, standard deviation; UICC, Union for International Cancer Control.

Characteristic	Patients
Surgical procedure, n (%)	11 (9.4)
Cholecystectomy	1 (0.9)
Bile duct resection without liver resection	7 (6.0)
Type of liver resection	1 (0.9)
Liver bed resection	11 (9.5)
Partial hepatectomy	6 (5.2)
Subsegmentectomy	31 (26.7)
Sectionectomy	3 (2.6)
Hemihepatectomy	43 (37.1)
Trisectionectomy	2 (1.7)
Pancreaticoduodenectomy	
Hepatopancreaticoduodenectomy	
Operation time (min), mean ± SD (range)	457.3 ± 170.4 (124–1 049)
Blood loss (mL), mean ± SD (range)	770.1 ± 1 501.5 (10–13 870)
Blood transfusion, n (%)	15 (12.8)
T-stage (1/2/3/4)	18/40/51/8
N-stage (1), n (%)	48 (41.0)
UICC stage (sixth edition) (0/I/II/III/IV)	3/17/49/31/16
Resection (R0/R1/R2)	99/15/3
Lymph node metastasis (absent/present)	48/69
Tumor differentiation	44/32/9/7/5/7/13
Well/moderate/poor/pap/well-pap/other/unknown	
Mortality, n (%)	1 (0.9)
Postoperative adjuvant chemotherapy, n (%)	78 (66.7)
Postoperative complications (Clavien–Dindo grade ≥ 3a) (absent/present)	44/73

BMI, body mass index; CA19-9, carbohydrate antigen 19 – 9; CEA, carcinoembryonic antigen; CRP, C-reactive protein; PNI, prognostic nutritional index; SD, standard deviation; UICC, Union for International Cancer Control.

Relationship between clinicopathological variables and the PNI

Table 2 shows the relationship between clinicopathological variables and the PNI. Patients in the low PNI group had a significantly longer mean operation time than those in the high PNI group (513 ± 216 *vs.* 438 ± 149 minutes, respectively; $P = 0.042$). A significantly higher proportion of patients had lymph node metastasis in the low PNI group than in the high PNI group.

Table 2
Clinicopathological characteristics according to the PNI

Characteristic	High PNI (PNI ≥ 42) (n = 88)	Low PNI (PNI < 42) (n = 29)	*P*-value
Age (years), mean ± SD	73.5 ± 9.1	75.5 ± 10.8	0.329
Sex (male/female)	54/34	19/10	0.688
BMI (kg/m^2)	22.6 ± 3.4	21.9 ± 4.3	0.347
CEA level (ng/mL), mean ± SD	6.35 ± 14.90	4.85 ± 4.24	0.593
CA19-9 level (U/mL), mean ± SD	1 072.7 ± 4 565.5	835.6 ± 2 484.6	0.790
Preoperative cholangitis (absent/present)	58/30	15/14	0.175
Comorbidities (absent/present)	25/63	9/20	0.788
Type of cancer (ICC/other)	23/65	7/22	0.830
Resection (R0–1/R2)	77/11	22/7	0.148
Operation time (min), mean ± SD	438 ± 149	513 ± 216	0.042 *
Blood loss (mL), mean ± SD	717 ± 1 560	929 ± 1 319	0.512
Transfusion (no/yes)	77/9	23/6	0.154
T-stage (≥ 3), n (%)	43 (48.9)	16 (55.2)	0.555
N-stage (1), n (%)	30 (34.1)	18 (62.7)	0.008 **
UICC stage (sixth edition) (I–II/III–IV)	56/32	13/16	0.076
Tumor differentiation (well/other)	37/51	12/17	0.945
Postoperative complications (Clavien–Dindo grade ≥ 3a) (absent/present)	56/32	17/12	0.630
Postoperative adjuvant chemotherapy (no/yes)	28/60	9/20	0.927

* $P < 0.05$; ** $P < 0.01$.

BMI, body mass index; CA19-9, carbohydrate antigen 19 − 9; CEA, carcinoembryonic antigen; ICC, intrahepatic cholangiocarcinoma; PNI, prognostic nutritional index; SD, standard deviation; UICC, Union for International Cancer Control.

Univariate and multivariate analyses of clinicopathological factors affecting OS after surgical resection

The median OS time was 48.8 (range, 1–120) months. The 1-, 3-, and 5-year OS rates were 85.9%, 57.8%, and 46.9%, respectively. In the Kaplan–Meier analysis of all patients, the low PNI group had a

significantly shorter OS time than the high PNI group ($P = 0.004$; Fig. 1). Table 3 shows the relationship between clinicopathological variables and OS after surgical resection. In univariate analysis, OS was significantly worse in patients with lymph node metastasis ($P < 0.001$), carbohydrate antigen 19 – 9 levels ≥ 20 U/mL ($P = 0.009$), preoperative cholangitis ($P = 0.049$), tumor differentiation ($P = 0.006$), an operation time ≥ 360 minutes ($P = 0.027$), and R1–2 resection ($P = 0.001$). Multivariate analysis showed that a low PNI (< 42) ($P = 0.007$), lymph node metastasis ($P = 0.024$), and tumor differentiation ($P = 0.008$) were significant independent predictors of OS.

Table 3
Univariate and multivariate analyses of clinicopathological factors affecting OS after resection of BTC

Factor	Univariate analysis		Multivariate analysis	
	n	*P*-value	HR (95% CI)	*P*-value
Age (years)	60	0.827	–	–
≥ 75	57			
< 75				
Sex	73	0.134	–	–
Male	44			
Female				
BMI (kg/m^2)	81	0.528	–	–
≥ 20	36			
< 20				
CEA level (ng/mL)	17	0.894	–	–
≥ 9	100			
< 9				
CA19-9 level (U/mL)	57	0.009 **	1.22 (0.63–2.39)	0.559
≥ 20	60			
< 20				
Preoperative cholangitis	44	0.049 *	1.23 (0.67–2.22)	0.493
Present	73			
Absent				
Comorbidities	83	0.118	–	–
Present	34			
Absent				

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

BMI, body mass index; BTC, biliary tract cancer; CA19-9, carbohydrate antigen 19 – 9; CEA, carcinoembryonic antigen; CI, confidence interval; HR, hazard ratio; ICC, intrahepatic cholangiocarcinoma; OS, overall survival; PNI, prognostic nutritional index.

Factor	Univariate analysis		Multivariate analysis	
	n	*P*-value	HR (95% CI)	*P*-value
Type of cancer	30	0.119	–	–
ICC	87			
Other				
Resection	99	0.001 **	1.28 (0.61–2.56)	0.502
R0	18			
R1–2				
Operation time (min)	83	0.027 *	1.13 (0.545–2.50)	0.750
≥ 360	34			
< 360				
Blood loss (mL)	82	0.475	–	–
≥ 200	35			
< 200				
Transfusion	99	0.432	–	–
No	15			
Yes				
T-stage	58	0.002 **	1.72 (0.85–3.57)	0.130
< 3	59			
≥ 3				
N-stage	69	< 0.001 ***	2.11 (1.10–4.08)	0.024 *
0	48			
1				

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

BMI, body mass index; BTC, biliary tract cancer; CA19-9, carbohydrate antigen 19 – 9; CEA, carcinoembryonic antigen; CI, confidence interval; HR, hazard ratio; ICC, intrahepatic cholangiocarcinoma; OS, overall survival; PNI, prognostic nutritional index.

Factor	Univariate analysis		Multivariate analysis	
	n	*P*-value	HR (95% CI)	*P*-value
Tumor differentiation	49	0.006 **	2.32 (1.24–4.52)	0.008 **
Well	68			
Other				
PNI	29	0.002 **	2.42 (1.29–4.42)	0.007 **
< 42	88			
≥ 42				
Postoperative complications (Clavien–Dindo grade ≥ 3a)	73	0.476	–	–
Absent	34			
Present				
Postoperative adjuvant chemotherapy	37	0.676	–	–
No	80			
Yes				
* *P*< 0.05; ** *P*< 0.01; *** *P*< 0.001.				
BMI, body mass index; BTC, biliary tract cancer; CA19-9, carbohydrate antigen 19 − 9; CEA, carcinoembryonic antigen; CI, confidence interval; HR, hazard ratio; ICC, intrahepatic cholangiocarcinoma; OS, overall survival; PNI, prognostic nutritional index.				

Combined prediction model

A simple scoring system was developed for all patients, with 1 point assigned to each significant factor (a low PNI [< 42], lymph node metastasis, and tumor differentiation) using similar odds ratios as those reported in the multivariate analysis. Patients were divided into four groups (0, 1, 2, and 3) according to the number of risk factors. The proportion of patients in each group who survived was significant (*P*< 0.001; Fig. 2a). Predictive power was compared using the AUC values for each point in the scoring system (1 point, AUC = 0.652; 2 points, AUC = 0.595; 3 points, AUC = 0.722). The AUC values for 1 and 3 points in the scoring system were larger than the AUC value for the PNI alone (AUC = 0.613; Fig. 2b). A combined score of the PNI and pathological findings outperformed each marker alone, in terms of discriminatory ability.

Discussion

In this study, we showed that the PNI is associated with poor prognosis after surgical resection in patients with BTC, consistent with a previous report [7]. Tumor-related factors, including lymph node metastasis and tumor differentiation, were also found to be independent prognostic factors in multivariate analysis. Based on these findings, we developed a novel inflammation-based prognostic scoring system combining the PNI and pathological findings, which proved to be more effective than either marker alone.

A meta-analysis [16] showed that the PNI could be used as an independent prognostic marker for patients with BTC. Moreover, elevated neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios may be unfavorable prognostic factors for clinical outcomes in patients with BTC [17].

The PNI, which is calculated using serum albumin concentration and total lymphocyte count, reflects the nutritional and immunological status of patients with cancer, and is a potential prognostic factor for survival. The mechanisms underlying the prognostic significance of the PNI in patients with BTC are discussed below.

Systemic inflammation has been shown to play an important role in cancer growth, invasion, and metastasis [18]. Total lymphocyte count is a component of the PNI. CD4 + and CD8 + T lymphocytes are major components of the immune microenvironment [19]. Tumor-infiltrating CD4 + and CD8 + T lymphocytes induce apoptosis and inhibit cancer cell proliferation [20]. Hence, lymphocytes play a critical role in cell-mediated antitumor immunity and immune surveillance [21]. Low lymphocyte counts lead to an insufficient immunological response in the tumor microenvironment, promoting cancer progression.

Malnutrition is common in patients with cancer [22], and has a negative impact on survival and recovery. Serum albumin concentration in the PNI reflects the nutritional status of patients with cancer. A low serum albumin concentration is associated with malnutrition and weight loss [23]. Hypoalbuminemia is not only a syndrome of poor nutritional status, but is also associated with a weakened host immune system [24]. Thus, a low serum albumin concentration usually predicts poor prognosis in patients with cancer. A low PNI may be predictive of an unfavorable prognosis in patients with BTC due to the aforementioned reason.

As discussed above, a low PNI may reflect systemic inflammation and progressive nutritional decline, resulting in poor survival. Perioperative nutritional support is recommended to improve the nutritional status of patients with hepatobiliary pancreatic carcinoma who have a high prevalence of malnutrition [25]. Preoperative immunonutrition has been reported to suppress the perioperative inflammatory response [26]. Further studies evaluating the relationship between immunonutrition and this inflammation-based prognostic score are required to improve the management of patients with BTC with a low PNI.

It is well known that clinicopathological characteristics, such as lymph node metastasis and tumor differentiation, significantly affect the prognosis of patients with cancer. Independent prognostic factors in this study included lymph node metastasis and tumor differentiation. Previous studies [27, 28] have shown that tumor differentiation is a predictor of survival after curative resection of BTC. In this study,

patients with well-differentiated tumors had significantly longer survival times than those with other histologies. This was further confirmed by multivariate analysis. These findings suggest that tumor differentiation is a predictor of long-term survival. Patients with poorly differentiated tumors should be carefully monitored during postoperative follow-up to detect recurrence early.

Clinicopathological predictors have proven to be suboptimal for identifying high-risk patients. Recent evidence has underscored the discriminatory power of a combined prognostic index. Pinato *et al.* [29] proposed a new prognostic score for hepatocellular carcinoma based on a combination of the modified Glasgow prognostic score and the Cancer of the Liver Italian Program score. They reported that the predictive accuracy of the combined score was superior to that of the Cancer of the Liver Italian Program score alone. Lin *et al.* [30] combined the lymphocyte-to-monocyte ratio and pathological TNM stage to establish the inflammation-based pathological stage. They showed that the inflammation-based pathological stage was superior to either the pathological TNM stage or inflammation-based index alone. There are few established staging systems for BTC. In this study, we showed that the prognostic power of a combined scoring system may be more effective than the PNI alone. Our combined scoring system accurately predicted prognosis and can be applied as a novel prognostic indicator for patients with BTC.

The PNI was associated with several clinicopathological factors in this study. A low PNI was associated with lymph node metastasis and a longer operation time, suggesting that patients with a low PNI are at high risk of advanced disease.

This study has several limitations related to its single-center retrospective design and small sample size. The sample size limited the statistical power of multivariate and subgroup analyses. The study population was heterogeneous in terms of diagnosis and type of resection. The OS rates differed for each type of BTC (ICC, GBC, extrahepatic cholangiocarcinoma, etc.), although not statistically significant. Most patients underwent radical resection. However, in patients with early-stage GBC, less invasive resections, such as cholecystectomy and liver bed resection, were more commonly performed. Future prospective multicenter studies with larger sample sizes are needed to validate our findings.

Conclusions

A high PNI (≥ 42), lymph node metastasis, and tumor differentiation were independent prognostic factors for OS after surgical resection in patients with BTC. Our simple and convenient scoring system will help refine patient stratification and predict survival. In addition, a novel and powerful inflammation-based scoring system was developed. Determining indications for nutritional support with immunonutrition and more intensive follow-up or postoperative treatment, such as chemotherapy and radiotherapy, is needed for patients with a high PNI (≥ 42).

Abbreviations

AUC, area under the receiver operating characteristic curve; BTC, biliary tract cancer; GBC, gallbladder carcinoma ICC, intrahepatic cholangiocarcinoma; OS, overall survival; PNI, prognostic nutritional index; TNM, Tumor–Node–Metastasis.

Declarations

Ethics approval and consent to participate:

The study was approved by the Ethical Review Board of the National Hospital Organization Fukuyama Medical Center (Hiroshima, Japan) (approval number: R2-34). Informed consent was obtained from all individual participants included in the study. We confirmed that all methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication:

Not applicable.

Availability of data and materials:

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests:

The authors declare that they have no competing interests.

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Authors’ contributions:

MU, TK, KK, NT, YY, YU, TN, RH, HM, YT, SO, and MI designed the study. MI, MU, NT, and KK treated and observed the patients. MU prepared the manuscript and performed the literature search. MI corrected and revised the manuscript. All authors read and approved the final manuscript.

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Figures

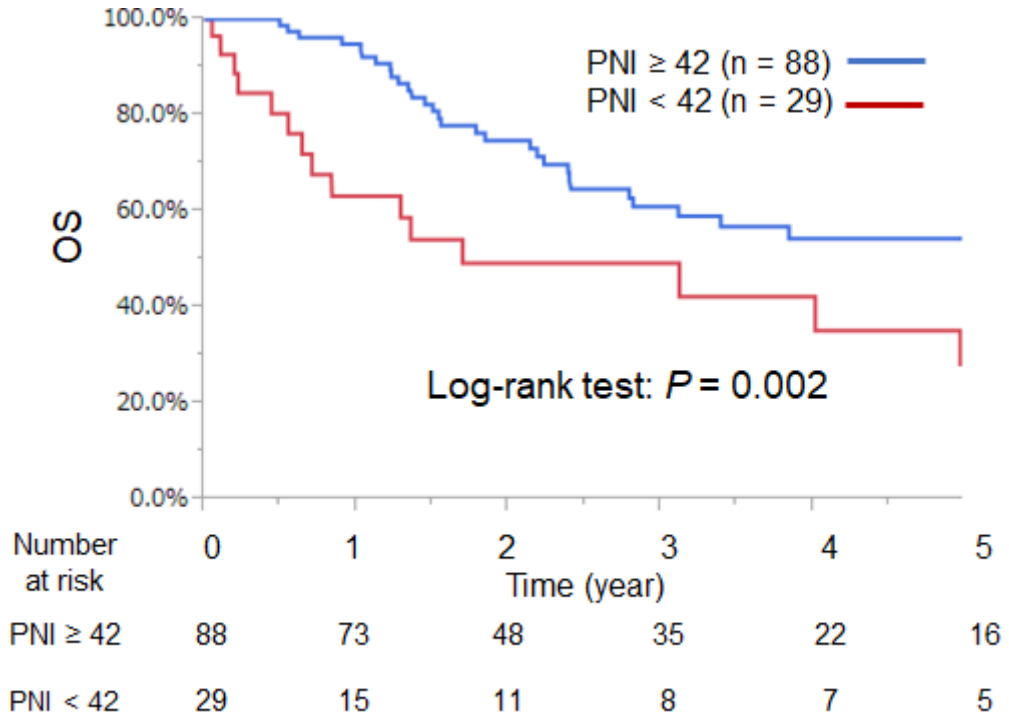

Figure 1

Kaplan–Meier curves of OS after resection of BTC in patients stratified by the PNI. BTC, biliary tract cancer; OS, overall survival; PNI, prognostic nutritional index.

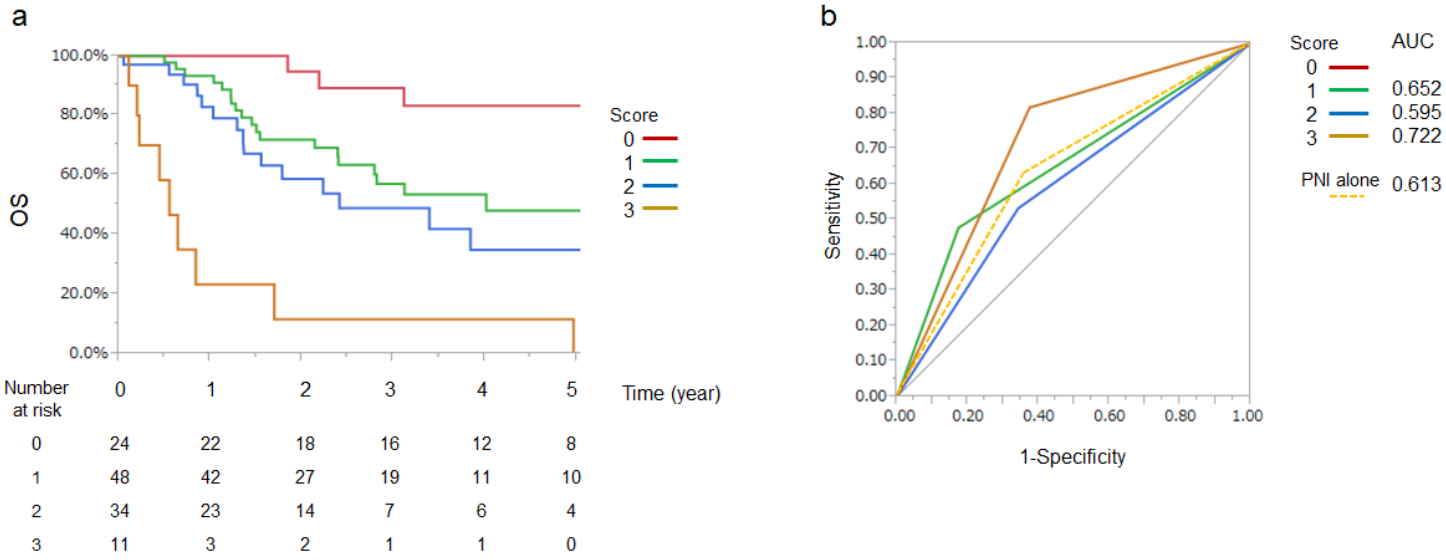

Figure 2

Combined prediction model. (a) Kaplan–Meier curves of OS according to the following scoring system, with 1 point assigned to each significant factor using similar odds ratios as those reported in the multivariate analysis: PNI < 42, lymph node metastasis, and tumor differentiation. Patients were divided into four groups (0, 1, 2, and 3) according to the number of risk factors. The proportion of patients in each group who survived was significant ($P < 0.001$). (b) Receiver operating characteristic curves of the scoring system. Predictive power was compared using the AUC for each point in the scoring system. AUC, area under the curve; OS, overall survival; PNI, prognostic nutritional index.